Proceedings of a Joint Meeting held between The Norwegian Society of Infectious Diseases and the Royal Society of Tropical Medicine and Hygiene, Oslo, 20th June 2008

Article (Unspecified)

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Introduction

The Royal Society of Tropical Medicine and Hygiene (RSTMH) has a tradition of holding joint meetings with fellow European Societies, providing opportunities to facilitate discussion, exchange information, foster mutual interests and develop collaboration between the societies' members and fellows. This paper presents the proceedings from a scientific meeting that was held between The RSTMH and the Norwegian Infectious Diseases Society at Ulleval University Hospital, Oslo on 20th June 2008. Three speakers from each society gave state-of-the-art lectures in their areas of expertise and the meeting ended with a series of case presentations.

Tore Godal: "Norway's commitments to maternal and child health"

Dr Godal, an international public health specialist who has worked with the Bill and Melinda Gates Foundation, the World Health Organisation and the Global Alliance for Vaccines and Immunisation (GAVI), focussed on progress towards achieving the 4th and 5th Millennium Development Goals (MDGs); reduction of child mortality and improving maternal health. Dr Godal described the impact of the GAVI programme on childhood mortality: between 2003-2007 the number of children vaccinated per annum rose from 40 million to 170 million, which translated into an estimated rise in lives saved through vaccination from 0.7 to 2.9 million. Dr Godal outlined the considerable funding that the Norwegian Government has committed, working in partnership with other organisations such as the World Bank, towards meeting the MDGs. The MDG strategy was reviewed, noting that goals 4 and 5 are not on target to achieve their aims by 2015. Indeed, in the Africa region the under-5 mortality

rate is increasing. Least progress has been made in neonatal mortality. Data presented at this meeting indicated that there are over 10 million neonatal, child and maternal deaths per annum globally. Of these, 0.5 million are maternal deaths, there are 2 million neonatal deaths on day 1 of life, 2 million neonatal deaths in the first month of life and 1.6 million other children die under the age of 5. 2.5 million of these deaths are vaccine preventable. There are packages in place to address the causes of mortality such as safe delivery, childcare packages, and vaccination campaigns not only to ensure currently available vaccines are widely administered but also to develop new vaccines against diseases such as rota virus and pneumococcal.

A scheme was described whereby women in Rajasthan, India, were paid between $30-50 to deliver in a clinic. The numbers of women who delivered in clinic rose from 0.92% in 2004/5 to 76% in 2006/7. This had a major beneficial impact on maternal and neonatal mortality. One of the important factors in the success of this scheme was the support of senior political leaders.

Gail Davey: "Recent advances in podoconiosis: aetiology and consequences"

Podoconiosis (endemic non-filarial elephantiasis) is a neglected tropical disease that affects up to 5% of the population in endemic areas, where it can be more prevalent than HIV/AIDS or malaria. However, the medical and scientific communities are often unaware of the existence of the disease despite the fact that it is a preventable disease.

A historical overview was given; podoconiosis may have been described as elephantiasis 'of the Arabs' by Rhazes, a Persian physician who taught in Baghdad *c.*905. Over time further references to podoconiosis were made in the literature, but it was not until the 1960's and 1970's that the disease was characterised in more detail through the work of Ernest Price and others working in Ethiopia particularly. He described the natural history and distribution of the disease, and started to investigate its aetiology. Podoconiosis is a disease of the impoverished. Development of disease requires exposure to a particular type of red clay soil that is volcanic in origin, occurs in regions of high seasonal rain fall, high altitude and low income.

Systematic baseline epidemiological and clinical studies by Dr Davey and her colleagues in the Wolaita Zone of southern Ethiopia have provided a firm basis for further research on the aetiology and consequences of podoconiosis, where most of the recent advances described by Dr Davey have occurred. A programme of research into the genetic basis of the disorder in Ethiopia has begun. Following the observation that cases of podoconiosis cluster in families, further studies suggested that it is a heritable disease with an autosomal co-dominant gene inheritance. Work has also been undertaken towards defining the biochemical and immunological abnormalities underlying the inflammation and fibrosis that lead to pathology.

In terms of the consequences, research into the economic effects has shown that podoconiosis worsens the already dire economic situation of individuals who have the disease. Furthermore, it is a highly stigmatising disease which excludes sufferers from religious and social functions and marriage. This research is ongoing and a number of collaborators are involved with this

project both locally and internationally including the Mossy Foot Treatment and Prevention Association, a non-governmental organisation based in the heart of the Wolaita community.

Eyrun Kjetland: "Treatment of schistosomiasis as an intervention against HIV infection in Africa".

200 million people in 76 countries have schistosomiasis and 85% of these indovodials live on the African continent. Women may have genital schistosomiasis caused by any of the Schistosoma species without symptoms in the urinary tract. It has been estimated that 5-10% of female genital schistosomiasis affects the ovaries, 10-30% the fallopian tubes, 1-5% the uterus, 60-80% the cervix and 40-60% the vagina. Schistosomiasis may also occur in the external genital region. Dr Kjetland described the typical appearances of genital schistosomiasis seen on colposcopy in female patients. These include a yellow grainy appearance, contact bleeding and neovascularisation. There is much overlap between the geographical distribution of schistosomiasis and HIV in sub-Saharan African countries such as Zimbabwe where Dr Kjetland is conducting her research. Groups at particular risk of co-infection are those with commuting spouses, those living in road side villages or newcomers to the cities. Genital ulcers caused by syphilis and herpes have been hypothesised to increase the transmission of HIV. However, genital schistosomiasis has been overlooked in this context. Regression analysis of risk factors for HIV infection has shown an association with increasing age, widowhood, infertility and co-infection with type II Herpes simplex virus, syphilis and human papilloma virus. The presence of

schistosomal ova in cervical smears was also associated with HIV infection. The demography of schistosomiasis suggests that schistosomal infection precedes HIV infection as it occurs in all age groups including younger children who are not sexually active. In some regions genital schistosomiasis is the commonest genital lesion. It is not clear how the two infections interact at a molecular level but there is evidence that schistosomiasis may increase the expression of chemokine receptors that are co-receptors for HIV on peripheral blood mono-nuclear cells.

Dr Kjetland went on to describe a retrospective and a prospective exploration of treatment. In the retrospective analysis treatment women who had been treated early were found to have significantly less contact bleeding and sandy patches than women who had been treated after the age of 20 years. Furthermore these findings were independent of the current waterbody contact. In the prospective analysis women were given a single dose of praziquantel and were followed up at 3 months. The two groups (treated and untreated) were the given either one more dose or not. A third dose was given at 12 months and assessed after 25 months. The results of the latter investigation are not conclusive and further, larger studies are required.

Diana Lockwood: "Diagnosing leprosy in a cold climate 1995-2008"

Dr Lockwood spoke about her experience of leading the major leprosy referral centre in the United Kingdom. In London leprosy is an important imported disease and early diagnosis is essential to ensure the best treatment is given

as soon as possible to prevent permanent consequences such as nerve damage.

A review of the pathology of leprosy was presented describing how the polarised immune response correlates with the clinical phenotype, ranging from tuberculoid leprosy where there is strong cell mediated immunity and few organisms seen on microscopy through borderline leprosy to lepromatous leprosy where the immune response is predominantly humoral involving the production of antibodies rather than cell mediated immunity and is associated with large numbers of bacteria.

A retrospective review of 180 patients whose leprosy had been diagnosed in the UK was presented. There were three groups of patients; those in whom a new diagnosis of leprosy had been made, those who were being referred for management of complications or review following treatment and those who had been treated previously and were under follow-up. Data collected included the country where leprosy was acquired, when the patient arrived in the UK, the time until diagnosis, the clinical type of leprosy and the complications experienced by patients.

Over half of the cases came from the Indian subcontinent and approximately equal numbers came from Africa, South East Asia and the Americas. A small percentage of cases were born in the UK and cases patients had been resident in leprosy endemic areas are between 8-48 years. Recently increasing numbers of Brazilians have been seen with leprosy and this reflects changes in migration patterns. The commonest referral patterns were from dermatologists and neurologists but also rheumatologists, orthopaedic

surgeons, infectious disease clinicians and others referred cases. Paradoxically, leprosy appears to be easier to diagnosis in resource-poor endemic regions than the UK as significant delays in diagnosis in the UK: the median time until diagnosis was approximately 2 years. Diagnosis was delayed because the diagnosis was not recognised by health care professionals, or for patient-related reasons, but more commonly delay was due to misdiagnosis. Nerve involvement was common at presentation and approximately 1/3 of patients had leprosy reactions. The main conclusion from this talk was to always consider leprosy especially in patients with unexplained neuropathy, ulcers and skin lesions.

Peter Chiodini: "Challenges in the deployment of new malaria diagnostics"

Rapid diagnostic tests (RDTs) for malaria are antigen detection tests used to diagnose the presence of malaria parasites in the blood using a fingerprick sample. Some detect *Plasmodium falciparum* only, others can detect the other species that cause human disease. They have important potential in the management of malaria in countries where malaria is endemic: such countries generally lack resources and access to good quality microscopy (the conventional tool used for diagnosing malaria) is often lacking. In this context, RDTs are used in settings where the ambient temperatures are high and the logistics of delivery of medical supplies to more rural health care facilities may be difficult. The stability of the product and long length of shelf-life are important parameters to consider when developing and assessing RDTs.

Since they are designed for field use they should be simple to use. Given the issues around quality control, the WHO has set target sensitivities for RDTs and has a programme for RDT evaluation.

In June 2008 there were 30 manufacturers marketing 88 products which come in a variety of forms including dipsticks, cassettes and cards. There is much variation in the performance of RDTs but both between products and between locations where they are being used. A number of other factors can also influence the test result including the condition of the devices, the quality of their technique and test interpretation. Professor Chiodini highlighted a few of these in more detail. Concerns have been raised about the conditions that RDTs are stored in, in countries where malaria is endemic. Thus, for most the recommended storage temperature is between 4-30ºC and most the majority of RDTs have a recommended shelf life of up 18 to 24 months, reflecting the fact that these tests have been developed and tested in temperate climates. However, the ambient temperature is often higher than 30ºC in many malaria endemic countries and this leads to concerns about the viability of these tests in such conditions.

The parasite under detection also has an influence on the performance of the test. In addition to the different species, different tests detect structurally different antigens and the antigen may persist after treatment in some cases.

RDTs are being used more frequently in the UK as well and appear to be replacing microscopy out of normal working hours in units where experience is limited.

In conclusion, these tests have the potential to transform the diagnosis of malaria in the tropics, but meticulous quality control is paramount.

Gunnar Bjune: "The importance of diagnostic delay in tuberculosis control"

Dr Bjune began with an overview of the changing epidemiology of tuberculosis (TB), describing how the incidence of the disease fell until the early 1980's but since then there has been a global increase in the number of cases of TB. The epidemiology varies between high income and low income regions of the world and in high income countries the increase in TB is associated with immigration, urbanisation and an increasing marginalised society. There was also a lack of recognition of TB in such groups who access health care facilities infrequently. Treatment is often sub-optimal in these groups for a number of different reasons. In low income countries HIV co-infection plays a major role but TB is also associated with increased life expectancy, urbanisation, malnutrition and break down of health services. A surprising example of the lack of impact of "the classical" social risk factors is the increasing prevalence of TB in north-west Russia since the fall of the Soviet Union. Here the whole increase could in fact be explained by the introduction of "emerging successful stains" of *Mycobacterium tuberculosis* in to the area. In particular, the prisons had functioned as breeding sites for this expansion since 1992. In one prison in Archangels, Russia, large clusters of cases caused by the Beijing strain of *M. tuberculosis* were noted. It was evident that most of these strains were acquiring drug resistance without

losing fitness. A consortium named "TB in the 21st Century" came together to investigate this further.

Studies to date indicate that the Beijing strain is not responsible for the epidemic of TB in sub-Saharan Africa but plays a dominant role in South East Asia. These observations have led to the finding that, in experimental mice, the Beijing strain had lost the ability to develop stable latent TB. There is also increasing evidence that the BCG vaccine does not protect against the Beijing strain. A discussion of the evolution of *M. tuberculosis* focussed on the fact that it is causes chronic infection associated with latency and there are a number of selective forces at play including antibiotic treatment and BCG. *M. tuberculosis* has evolved through loss of genetic material and has acquired a number of mechanisms to escape host resistance.

Meanwhile, efforts are required to control the epidemic through preventing transmission. One of the barriers to this is the number of pulmonary TB cases slowly fighting their way toward a correct diagnosis. These patients are contributing the bulk of the infectious reservoir in the community. However, in populations where chronic cough is common and can have many aetiologies, how can we rapidly identify the individuals who really do have infectious smear positive TB to ensure they get treated more quickly? Such patients often have contact with health facilities at a relatively early stage in their history: a simple rapid diagnostic tool that identified the "true TB suspected cases" would be a major advance in TB control.

David Molyneux: “From donation to elimination: the Global Filariasis Programme ten years on”

Filariasis is endemic in 83 countries, there are 1.3 billion people at risk and 120 million people live with the disease. It is a leading cause of global disability, possibly second only to mental health disorders. There is stigma attached to the disease and social and economic consequences which impact on the affected individuals' access education and also marriage prospects. Filariasis has been recognised as one of six potentially eradicable infectious diseases by the International Task Force for Disease Eradication that was set up in 1993 to meet this target. The elimination strategy has involved multiple partners; donors, academia, non-governmental development organisations (NGDOs) and particularly endemic countries. The strategy has been to interrupt transmission through the use of the drugs diethylcarbamazine and albendazole in areas where onchocerciasis is not endemic and albendazole and ivermectin where there is onchocerciasis. Albendazole and ivermectin (Mectizan) are donated by GSK and Merck & Co. inc. respectively. The other arm of the programme is to alleviate and prevent disabilities. To date nearly 2 billion people have been treated within the context of this programme and one of the collateral benefits has been the treatment of hookworm, a major cause of anaemia globally other intestinal worms, and ectoparasites in areas where ivermectin is used. The disease has been mapped using rapid diagnostic tests and during the course of the campaign there has been a reduction of 83% of antigenemia in sentinel villages in Nigeria; a reduction of 83% of positive midnight bloods and a 92% reduction in infected mosquitoes. Following treatment interventions, monitoring and evaluation has been critical to determine when mass drug administration can be stopped. Several

countries are now evaluating if transmission has stopped -Egypt, Sri Lanka, Zanzibar and several Pacific island nations.

The meeting concluded with case presentations describing unusual manifestations of tropical diseases including babesiosis, dengue fever, genital schistosomiasis, leishmaniasis, hydatid disease and an outbreak of malaria.

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